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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,147	06/11/2001	Kenneth Kellar	NIDN-10	9771

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AMERSHAM BIOSCIENCES
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER

HARTLEY, MICHAEL G

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 08/04/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,147

Applicant(s)

KELLAR, KENNETH

Examiner

Michael G. Hartley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13,14,23 and 25-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13,14,23 and 25-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/19/2003 has been entered.

Response to Amendment

The amendment filed 6/19/2003 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to describe the specific negative limitation as inserted into claim 33, namely, "with the proviso that the aforementioned chelates do not comprise a hydroxyaryl group at the nitrogen atom" in section (a). It is noted that any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983) *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 13, 14, 23, 25-29, 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 5,368,840) in view of either one of Lauffer (US 5,250,285); or Hemmi (US 5,886,173) or Chiu (US 5,344,639).

Unger discloses a method of imaging diseased vasculature (i.e., which would encompass regions of decreased vascular perfusion) comprising administering an MRI contrast agent comprising a paramagnetic metal and a chelating agent, wherein the chelating agent may be those well known in art as being effective as MRI contrast agents. These chelating agents include those claimed, such as, DOTA, EDTA, DO3A, kryptands, etc., see column 6, lines 36-56. Unger also teaches that various metals may be used in an equivalent manner, including europium, i.e., Eu(III), see column 6, lines 30-65. The chelating agents may also be conjugated to targeting moieties, such as polymers, antibodies, etc., as claimed, see column 6, lines 30-65.

Unger fails to disclose that the paramagnetic metal used in Eu(II) as claimed. However, the use of Eu(II) as a paramagnetic metal for use in MRI contrast agents is known, as shown by any one of Lauffer, Hemmi or Chiu.

Lauffer discloses a method of imaging diseased vasculature, including perfusion thereof, (i.e., which would encompass regions of decreased vascular perfusion) comprising administering an MRI contrast agent comprising a physiologically tolerable Eu(II) compound, see abstract, column 1, lines 50-64 and column 6, line 10+.

Hemmi discloses MRI contrast agents comprising porphyrins, and other chelating agents that are conjugated with a paramagnetic metal, see abstract. Hemmi teaches that Eu (II) is known to be a useful

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paramagnetic metal for MRI that is equivalent to other metals, such as Eu(III), etc., (as disclosed by Unger, see column 6).

Chiu teaches metal complexes for methods of MRI and teaches that Eu (II) is known to be useful therefor and equivalent to other metals commonly employed in the art, see column 3.

It would have been obvious to one of ordinary skill in the art to modify the methods disclosed by Unger to have used Eu(II) as the Eu metal ion because it is well known in the art that Eu(II) is a useful paramagnetic metal species which is equivalent to other paramagnetic metal species for use in MRI to provide effective contrast enhancement, as shown by Lauffer, Hemmi and Chiu. Since Unger teaches that various metals may be employed in an equivalent manner, and since Eu (II) is a known equivalent metal for MRI as shown by Lauffer, Hemmi or Chiu, one of ordinary skill in the art would have been motivated to employ the known metal Eu(II) with the well known chelating agents, i.e., DOTA, kryptands in the methods disclosed by Unger. Also, the Eu(II) chelates formed from the above combination would have the functional properties defined in claims 23 and 25-27 since such are inherent characteristics of the contrast agents, e.g., relaxivities, changes in oxidative states and/or relaxivities by biological processes, etc.

Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 5,368,840) in view of either one of Lauffer (US 5,250,285); or Hemmi (US 5,886,173) or Chiu (US 5,344,639) as applied to claims 13, 14, 23, 25-29, 33 and 34 above, and further in view of Rocklage (US 5,190,744).

While Unger teaches that the MRI methods are useful for imaging various tissues, including tumors and/or the cardiovascular, they fail to specifically disclose that the methods are used for imaging the brain, such as, stroke, and the heart.

Rocklage teaches that MRI is especially useful for imaging decreased blood perfusion, and can provide a quantitative and temporal determination of perfusion for imaging stroke (i.e., the brain), as well as, cardiovascular perfusion abnormalities, etc., see column 2.

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It would have been obvious to one of ordinary skill in the art to employ the MRI methods disclosed by Unger, as modified by any one of Lauffer, Hemmi or Chiu for imaging decreased perfusion in various tissue, including, the brain (i.e., stroke), cardiovascular system, etc., (as claimed) because it is well known in the art that MRI is especially useful for imaging such tissues because it provides a quantitative and temporal determination of perfusion for imaging stroke (i.e., the brain), as well as, cardiovascular perfusion abnormalities, etc., as shown by Rocklage.


Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Michael G. Hartley
Primary Examiner
Art Unit 1616

MH
August 1, 2003